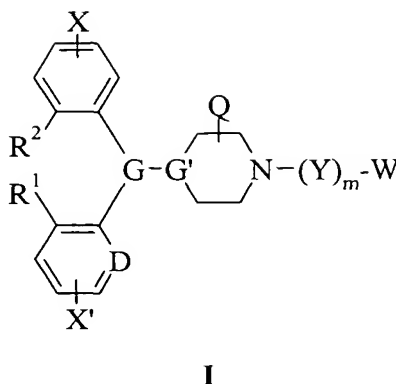


We Claim:

1. A compound of formula I:



and the geometrical isomers, enantiomers, diastereomers, and pharmaceutically acceptable salts thereof, wherein:

X and X' independently are hydrogen, halo, alkyl, alkenyl, alkynyl, alkoxy, trifluoromethyl or $-(Y')_m-W'$;

G and G' together form $\text{HC}-\text{N}$, $\text{HC}-\text{CH}$, or $\text{C}=\text{C}$;

D is $-\text{CH}=\text{}$ or $=\text{N}-$;

R^1 and R^2 independently are hydrogen or together are $-(\text{CH}_2)_n-$ in which n is equal to 0, 1, 2, or 3;

m and m' are independently 0 or 1;

Y and Y' are $-\text{L}^1-$ or $-\text{L}^2-\text{V}(\text{Z})_t-\text{L}^3-$ in which t is 0 or 1;

L^1 is alkylene, alkenylene, alkynylene, or one of the foregoing in which one or more methylenes are replaced by $-\text{O}-$, $-\text{S}-$, $-\text{S}(\text{O})-$, $-\text{S}(\text{O})_2-$, $-\text{N}(\text{Q})-$, or $-\text{N}(\text{R}^3)-$;

L^2 is (a) alkylene, alkenylene, alkynylene, or one of the foregoing in which one or more methylenes are replaced by $-\text{O}-$, $-\text{S}-$, $-\text{S}(\text{O})-$, $-\text{S}(\text{O})_2-$, $-\text{N}(\text{Q}')-$, or $-\text{N}(\text{R}^4)-$, or (b) $-\text{L}^4-\text{C}(\text{O})-\text{N}(\text{Q}')-$ or $-\text{L}^4(\text{Q}')-$, or (c) a direct bond;

L^3 is (a) alkylene, alkenylene, alkynylene, or one of the foregoing in which one or more methylenes are replaced by $-\text{O}-$, $-\text{S}-$, $-\text{S}(\text{O})-$, $-\text{S}(\text{O})_2-$, $-\text{N}(\text{Q}'')-$, or $-\text{N}(\text{R}^5)-$, or (b) a direct bond;

L^4 is (a) alkylene; alkenylene, alkynylene, or one of the foregoing in which one or more methylenes are replaced by $-\text{O}-$, $-\text{S}-$, $-\text{S}(\text{O})-$, $-\text{S}(\text{O})_2-$, $-\text{N}(\text{Q}'')-$, or $-\text{N}(\text{R}^5)-$, or (b) a direct bond;

V is (a) a divalent arene, a divalent heteroarene, or a divalent saturated heterocycle when t is 0, or (b) a trivalent arene or trivalent heteroarene when t is 1;

Q, Q', and Q'' independently are hydrogen, $-\text{AC}(\text{O})\text{OR}^6$, or $-\text{AC}(\text{O})\text{NR}^6\text{R}^7$;

W and W' independently are $-N(OM)C(O)N(R^8)R^9$, $-N(R^8)C(O)N(OM)R^9$, $-N(OM)C(O)R^8$, $-C(O)NR^8R^9$, or $-C(O)OR^8$, provided that at least one of W and W' is $-N(OM)C(O)N(R^8)R^9$, $-N(R^8)C(O)N(OM)R^9$, or $-N(OM)C(O)R^8$.

Z is $-A''N(OM')C(O)N(R^{10})R^{11}$, $-A''N(R^{10})C(O)N(OM')R^{11}$, $-A''N(OM')C(O)R^{11}$, $-A'C(O)N(OM')R^{11}$, $-A'C(O)NR^{10}R^{11}$, $-A'C(O)OR^{10}$, halo, CH_3 , NR^3R^4 , $NR^3C(O)R^4$, NO_2 , CN , CF_3 , $S(O)_2NR^3R^4$, $S(O)_2R^3$, SR^3 , or $S(O)R^3$.

A, A' and A'' independently are a direct bond, alkylene, alkenylene, alkynylene, yloalkylaryl, yloarylalkyl, or diylalkylarene or one of the foregoing in which one or more methylenes are replaced with $-O-$, $-NH-$, $-S-$, $-S(O)-$, or $-S(O)_2-$ and/or one or more methylenes are replaced by $=N-$;

M and M' independently are hydrogen, a pharmaceutically acceptable cation, or a metabolically cleavable group; and

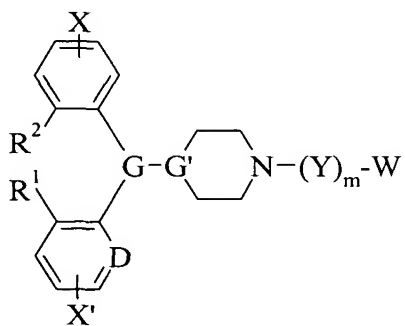
R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} , and R^{11} are independently hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkyl, alkylaryl, alkylarylalkyl, or one of the foregoing in which one or more methylenes are replaced by $-O-$, $-NH-$, $-S-$, $-S(O)-$, or $-S(O)_2-$ and/or one or more methylenes are replaced by $=N-$;

provided that, other than the oxygens bound to the sulfurs in $-S(O)-$ and $-S(O)_2-$, when one or more methylenes are replaced with $-O-$, $-NH-$, $-S-$, $-S(O)-$, or $-S(O)_2-$ and when one or more methylenes are replaced with $=N-$, such replacement does not result in two heteroatoms being covalently bound to each other;

and further provided that when m is 0, W is not $-C(O)NR^8R^9$, or $-C(O)OR^8$,

and further provided that in the substituent $-AC(O)OOR^6$, R^6 cannot be hydrogen when A is a direct bond.

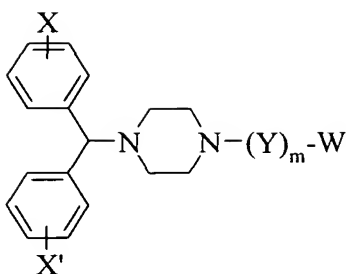
2. The compound of claim 1 having the formula I':



I

wherein the substituents are as defined in claim 1, and the geometrical isomers, enantiomers, diastereomers, and pharmaceutically acceptable salts thereof.

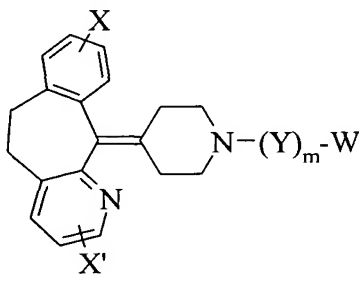
3. The compound according to claim 1 having the formula II:



II

wherein the substituents are as defined in claim 1, and the geometrical isomers, enantiomers, diastereomers, and pharmaceutically acceptable salts thereof.

4. The compound according to claim 1 having the formula **III**:



III

wherein the substituents are as defined in claim 1, and the geometrical isomers, enantiomers, diastereomers, and pharmaceutically acceptable salts thereof.

5. The compound according to claim 3 wherein X is -Cl, X' is hydrogen, m is 1 and W is -N(OH)C(O)NH₂.
6. The compound according to claim 4 wherein X is -Cl, X' is hydrogen, m is 1 and W is -N(OH)C(O)NH₂.
7. The compound according to claim 3 wherein X is -Cl, X' is hydrogen, m is 1, Y is -L¹-, wherein L¹ is alkynylene, yloalkoxy, or yloalkoxyalkyl.
8. The compound according to claim 4 wherein X is -Cl, X' is hydrogen, m is 1, Y is -L¹-, wherein L¹ is alkynylene, yloalkoxy, or yloalkoxyalkyl.
9. The compound according to claim 3 wherein X is -Cl, X' is hydrogen, m is 1, Y is -L²-V(Z)_t-L³-, t is 0, V is 1,4-phenylene or 1,3-phenylene, L² is yloalkoxy, and L³ is alkylene, alkenylene, or alkynylene.

10. The compound according to claim 4 wherein X is -Cl, X' is hydrogen, m is 1, Y is $-L^2-V(Z)_t-L^3-$, t is 0, V is 1,4-phenylene or 1,3-phenylene, L^2 is yloalkoxy, and L^3 is alkylene, alkenylene, or alkynylene.
11. The compound according to claim 3 wherein X is -Cl, X' is hydrogen, m is 1, Y is $-L^2-V(Z)_t-L^3-$, t is 0, V is 2,5-furylene, L^2 is alkylene, and L^3 is alkylene, alkenylene, or alkynylene.
12. The compound according to claim 4 wherein X is -Cl, X' is hydrogen, m is 1, Y is $-L^2-V(Z)_t-L^3-$, t is 0, V is 2,5-furylene, L^2 is alkylene, and L^3 is alkylene, alkenylene, or alkynylene.
13. The compound according to claim 3 wherein X is -Cl, X' is hydrogen, m is 1, Y is $-L^2-V(Z)_t-L^3-$, t is 1, L^2 is yloalkoxy, V is trivalent heteroarene, Z is $-A'C(O)NR^{10}R^{11}$ or $-A'C(O)OR^{10}$, and W is $-N(OH)C(O)NH_2$.
14. The compound according to claim 4 wherein X is -Cl, X' is hydrogen, m is 1, Y is $-L^2-V(Z)_t-L^3-$, t is 1, L^2 is yloalkoxy, V is trivalent heteroarene, Z is $-A'C(O)NR^{10}R^{11}$ or $-A'C(O)OR^{10}$, and W is $-N(OH)C(O)NH_2$.
15. The compound according to claim 3 wherein X and X' are F, m is 1, Y is $-L^2-V(Z)_t-L^3-$, t is 0, V is 1,4-phenylene or 1,3-phenylene, L^2 is yloalkoxy, and L^3 is alkylene, alkenylene, or alkynylene.
16. The compound according to claim 4 wherein X and X' are F, m is 1, Y is $-L^2-V(Z)_t-L^3-$, t is 0, V is 1,4-phenylene or 1,3-phenylene, L^2 is yloalkoxy, and L^3 is alkylene, alkenylene, or alkynylene.
17. A compound selected from the group consisting of compounds 1, 5, 11, 12, 13, 17, 23, 24, 31, 32, 33, 34, 35, 36, 37, 40, 41, 42, 43, 44, 45, 46, 48, 49, 50, 52, 53, 54, 55, 56, 57, 58, 59, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, and 94.
18. A compound selected from the group consisting of compounds 17, 32, 34, 35, 46, 52 and 80.
19. A compound according to claim 1 wherein
X and X' independently are hydrogen, halo or $-(Y')_m-W'$;
G and G' together form $\begin{array}{c} \diagup \\ HC-N \\ \diagdown \end{array}$, $\begin{array}{c} \diagup \\ HC-CH \\ \diagdown \end{array}$, or $\begin{array}{c} \diagup \\ C=C \\ \diagdown \end{array}$;

D is $-\text{CH}=\text{}$ or $=\text{N}-$;

R^1 and R^2 independently are hydrogen or together are $-(\text{CH}_2)_2-$;

m and m' are independently 0 or 1;

Y and Y' are $-\text{L}^1-$ or $-\text{L}^2-\text{V}(\text{Z})_t-\text{L}^3-$ in which t is 0 or 1;

L^1 is alkylene, alkenylene, alkynylene, or one of the foregoing in which one or more methylenes are replaced by $-\text{O}-$;

L^2 is (a) alkylene, alkenylene, alkynylene, or one of the foregoing in which one or more methylenes are replaced by $-\text{O}-$ or $-\text{N}(\text{Q}')-$ or (b) $-\text{L}^4-\text{C}(\text{O})-\text{N}(\text{Q}')-$;

L^3 is (a) alkylene, alkenylene, alkynylene, or one of the foregoing in which one or more methylenes are replaced by $-\text{O}-$ or $-\text{N}(\text{Q}'')$;

L^4 is alkylene;

V is (a) a divalent arene, a divalent heteroarene, or a divalent saturated heterocycle when t is 0, or (b) a trivalent arene or trivalent heteroarene when t is 1;

Q is hydrogen;

Q' , and Q'' independently are $-\text{AC}(\text{O})\text{OR}^6$, or $-\text{AC}(\text{O})\text{NR}^6\text{R}^7$;

W and W' independently are $-\text{N}(\text{OM})\text{C}(\text{O})\text{N}(\text{R}^8)\text{R}^9$, $-\text{N}(\text{R}^8)\text{C}(\text{O})\text{N}(\text{OM})\text{R}^9$, $-\text{N}(\text{OM})\text{C}(\text{O})\text{R}^8$, $-\text{C}(\text{O})\text{NR}^8\text{R}^9$, or $-\text{C}(\text{O})\text{OR}^8$, provided that at least one of W and W' is $-\text{N}(\text{OM})\text{C}(\text{O})\text{N}(\text{R}^8)\text{R}^9$, $-\text{N}(\text{R}^8)\text{C}(\text{O})\text{N}(\text{OM})\text{R}^9$, or $-\text{N}(\text{OM})\text{C}(\text{O})\text{R}^8$.

Z is $-\text{A}'\text{C}(\text{O})\text{NR}^{10}\text{R}^{11}$, $-\text{A}'\text{C}(\text{O})\text{OR}^{10}$, halo, $\text{NR}^3\text{C}(\text{O})\text{R}^4$, NO_2 , CN or CF_3 ;

A and A' independently are a direct bond, alkylene, alkenylene, alkynylene, or one of the foregoing in which one or more methylenes are replaced with $-\text{O}-$;

M and M' independently are hydrogen, a pharmaceutically acceptable cation, or a metabolically cleavable group; and

R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} , and R^{11} , if present, are independently hydrogen or alkyl in which one or more methylenes may be replaced by $-\text{O}-$;

provided that, other than the oxygens bound to the sulfurs in $-\text{S}(\text{O})-$ and $-\text{S}(\text{O})_2-$, when one or more methylenes are replaced with $-\text{O}-$, $-\text{NH}-$, $-\text{S}-$, $-\text{S}(\text{O})-$, or $-\text{S}(\text{O})_2-$ and when one or more methylenes are replaced with $=\text{N}-$, such replacement does not result in two heteroatoms being covalently bound to each other;

and further provided that when m is 0, W is not $-\text{C}(\text{O})\text{NR}^8\text{R}^9$, or $-\text{C}(\text{O})\text{OR}^8$,

and further provided that in the substituent $-\text{AC}(\text{O})\text{OOR}^6$, R^6 cannot be hydrogen when A is a direct bond.

20. A compound according to claim 19 wherein

X and X' independently are $-\text{H}$ or halo;

G and G' together form $\text{HC}-\text{N}$ or $\text{C}=\text{C}$;

Y is $-\text{L}^2-\text{V}(\text{Z})_t-\text{L}^3-$ in which t is 0 or 1;

L^2 is C_1 to C_6 alkylene in which one or more methylenes may be replaced by $-O-$

$V(Z)_t$ is phenylene optionally substituted by $-A'C(O)NR^{10}R^{11}$, $-A'C(O)OR^{10}$, halo, $NR^3C(O)R^4$, NO_2 , CN or CF_3 or furylene or oxolanylene;

L^3 is C_1 to C_6 alkylene in which one or more methylenes may be replaced by $-O-$ or C_2 to C_6 alkynylene;

W is $-N(OM)C(O)N(R^8)R^9$, $-N(R^8)C(O)N(OM)R^9$ or $-N(OM)C(O)R^8$

A' is methylene, vinylene or a direct bond.

R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} , and R^{11} , if present, are independently hydrogen or C_1 to C_6 alkyl in which one or more methylenes may be replaced by $-O-$.

21. A compound according to claim 20 wherein

X is fluorine or chlorine;

X' is hydrogen or fluorine;

Y is $-L^2-V(Z)_t-L^3-$ in which t is 0 or 1;

L^2 is C_1 to C_6 alkylene in which one methylene may be replaced by $-O-$

$V(Z)_t$ is phenylene optionally substituted by $-A'C(O)NR^{10}R^{11}$, $-A'C(O)OR^{10}$, halo, $NR^3C(O)R^4$, NO_2 , CN or CF_3 or furylene or oxolanylene;

L^3 is C_1 to C_6 alkylene in which one methylene may be replaced by $-O-$ or C_2 to C_6 alkynylene;

W is $-N(OH)C(O)NH_2$;

A' is methylene, vinylene or a direct bond

R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} , and R^{11} , if present, are independently hydrogen or C_1 to C_6 alkyl in which one methylene may be replaced by $-O-$.

22. A compound according to claim 1 wherein

X and X' independently are hydrogen, halo, alkyl, alkenyl, alkynyl, alkoxy or trifluoromethyl;

W is $-N(OM)C(O)N(R^8)R^9$, $-N(R^8)C(O)N(OM)R^9$ or $-N(OM)C(O)R^8$;

23. A compound according to claim 1 wherein

L^4 is alkylene

Z is $-N(OM')C(O)N(R^{10})R^{11}$, $-N(R^{10})C(O)N(OM')R^{11}$, $-N(OM')C(O)R^{11}$, $-A'C(O)N(OM')R^{11}$, $-A'C(O)NR^{10}R^{11}$ or $-A'C(O)OR^{10}$.

24. A compound according to claim 1 wherein

X and X' independently are $-H$, halo, alkyl, alkenyl, alkynyl, alkoxy or trifluoromethyl;

L^4 is alkylene

W is $-N(OM)C(O)N(R^8)R^9$, $-N(R^8)C(O)N(OM)R^9$ or $-N(OM)C(O)R^8$;

Z is $-N(OM')C(O)N(R^{10})R^{11}$, $-N(R^{10})C(O)N(OM')R^{11}$, $-N(OM')C(O)R^{11}$, $-A'C(O)N(OM')R^{11}$, $-A'C(O)NR^{10}R^{11}$ or $-A'C(O)OR^{10}$.

25. A compound according to claim 1 wherein when M or M' is a metabolically cleavable group this is selected from an organic or inorganic anion, a pharmaceutically acceptable cation, acyl, alkyl, phosphate, sulfate and sulfonate, $NH_2C(O)-$ or $(alkyl)OC(O)-$.

26. A compound according to claim 25 wherein acyl is $(alkyl)C(O)$, including acetyl, propionyl and butyryl.

27. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claims 1.

28. A method of simultaneously inhibiting both leukotriene- and histamine- mediated biological processes, the method comprising administering an effective leukotriene- and histamine- inhibiting amount of a compound according to claim 1 to a subject in need of such inhibition.

29. A method of treating asthma, seasonal and perennial allergic rhinitis, sinusitis, conjunctivitis, food allergy, scombroid poisoning, psoriasis, urticaria, pruritus, eczema, rheumatoid arthritis, inflammatory bowel disease, chronic obstructive pulmonary disease, thrombotic disease and otitis media, the method comprising administering to a patient suffering from asthma, seasonal and perennial allergic rhinitis, sinusitis, conjunctivitis, food allergy, scombroid poisoning, psoriasis, urticaria, pruritus, eczema, rheumatoid arthritis, inflammatory bowel disease, chronic obstructive pulmonary disease, thrombotic disease and otitis media, an amount of a compound according to claim 1 sufficient to reduce or eliminate the asthma.

30. A method according to claim 29 wherein the disease to be treated is selected from asthma and seasonal and perennial rhinitis.